

are already underway at the NIEHS, as part of the EMF *RAPID* (Electric and Magnetic Fields Research and Public Information Dissemination) Program. In fact, Program Director Gary Boorman reports, NIEHS researchers recently attempted to replicate the German study of breast cancer development in rodents. Boorman expects to see completed data from that study within 8 months. A second, two-year study involving 100 animals subjected to slightly lower chemical doses in conjunction with longer-term exposure to EMFs should also be completed soon, he says. "The NAS report was a good report," he says. "But it did not include many of the *RAPID* studies, because they didn't look at much data after 1994. We hope to prepare a report for Congress in 1998 that will allow us to examine the wealth of data produced since 1994."

The congressionally mandated NAS report—prepared by a 16-member committee including David A. Savitz, a professor at the University of North Carolina at Chapel Hill whose carefully controlled epidemiological studies have consistently suggested an association between EMFs and cancer—may deal another blow to a draft report of the National Council on Radiation Protection and Measurements (NCRP), which calls for a 2-milligauss limit on EMFs near day-care centers, schools, playgrounds, and newly built homes within the next 10 years. Portions of the draft appeared in the July/August 1995 issue of *Microwave News*, though it still has not cleared the NCRP's exhaustive peer-review process. "It seems to have entered an NCRP black hole," observed *MN* Editor Louis Slesin, who faults the NAS report for emphasizing the need for "conclusive" evidence of an EMF-related health hazard. "That's a very harsh burden," he said, adding that researchers have not conclusively ruled out EMFs as the cause of reported increases in childhood leukemia.

Until such questions are resolved, says Jack Sahl, a senior research scientist and manager of the Health Research and Evaluation Division at Edison International in Rosemead, California, utilities and policymakers would be wise to adopt "precaution-based" strategies for minimizing any possible health risks. [See *EHP* 104:908-911 (1996).]

For example, Sahl said in an interview, Edison International has prepared a manual offering common-sense guidelines for minimizing EMF exposure risks when designing new buildings. Similarly, since 1989, the California Department of Education has avoided building new schools in close proximity to high-voltage power lines.

No federal legislation is pending to limit EMF exposure, Sahl says, and policymakers who once championed exposure limits,

including Representative George Miller (D-California.), now seem to be backing away from the issue. The \$600,000 NAS report was requested by Representative Joseph M. McDade (R-Pennsylvania) in response to constituent concerns in Scranton, Pennsylvania, where a utility company wanted to install high-voltage power lines near homes. (McDade's press secretary, Jake O'Donnell, says the power company subsequently decided to relocate its power lines.) Though he hasn't identified a specific EMF research agenda, O'Donnell says, McDade will probably heed recommendations set forth by the NAS committee, which recommended more stringent epidemiological studies incorporating accurate measurements of magnetic fields inside homes and strategies for answering questions about childhood leukemia. The NAS report also recommended a host of biological studies. For example, the committee said, researchers should identify the mechanism by which EMFs seem to promote bone-healing in animals.

## New Protein Kinase Inhibitors

Swiss researchers are exploring a vast new sea of compounds that attack cancer cells at the genetic level. "Phenylamino-pyrimidines are a new class of potent and selective protein kinase inhibitors," said Jeurg Zimmermann, a project leader with the pharmaceutical division of CIBA-Geigy in Basel. The key to use of the phenylamino-pyrimidines (PAPs), Zimmermann said, is their selectivity. "A lot of compounds can attack protein kinases," he said, but if the compound doesn't select for specific enzymes, the subject cannot survive. PAPs tend to select certain protein kinases, such as protein kinase C (PKC), a calcium-dependent enzyme that is overexpressed in tumor cells. Throttling PKC with PAPs may result in the tumor being unable to grow or reproduce, and can possibly make it regress.

Zimmermann said another kinase that is commonly overexpressed in cases of glioblastoma, a usually fatal brain cancer, is platelet-derived growth factor receptor (PDGF-R). In some laboratory mice that have been implanted with glioblastoma tumors, the introduction of certain PAPs has brought the growth of the tumor to a standstill, has prevented other cells from developing the tumor, or has actually caused the tumor to regress, said Zimmermann.

Zimmermann and his colleagues chose to study the means of attacking the protein kinases, of which there are more than 200, because of the molecules' roles in signal transduction and cell proliferation, both of which are responsible for a cascade of events leading to cancer growth and metastasis in the body.

In a presentation at the American Chemical Society meeting in Orlando, Florida, Zimmermann demonstrated how rational drug design procedures, using pyrimidines—one of the main building blocks of DNA and RNA—have resulted in the synthesis of more than 500 compounds. Using pyrimidines as a base, scientists add various analogs to the pyrimidine until they discover a compound that looks as if it will attack a specific area of a cancer cell. Typically, scientists will develop numerous chemical varieties. Although "only about 10% of the compounds have shown any anticancer activity," Zimmermann said, several of the compounds that did limit tumor growth are now being studied further before they are tested in humans. "We have to test toxicity and pharmacokinetics to see if the drug gets into the bloodstream and can be of use therapeutically," he said.

"Rational drug design," said Theodore Friedmann, director of the gene therapy program at the University of California at San Diego, "is a common device utilized to manufacture chemicals that are likely to have an effect on treatment of some disease. Most drugs are developed using this procedure in laboratories, although other drugs are still commonly found by investigating organic compounds such as tropical earths."

By and large, Friedmann said, the use of rational drug design will result in an incremental increase in fighting a disease such as cancer. "We have hundreds of compounds that show some ability to fight cancer cells," he said, "which really testifies to the fact that we have very few drugs that really work well in destroying cancer cells. We use one for a while and when that stops working we go to another." But, he said, "occasionally something comes along that breaks the curve."

Zimmermann said he is encouraged that some of the PAPs being scrutinized by his team have shown a wide range of success on various tumors, including brain, breast, and bladder cell lines. More exciting, he said, is that some of the compounds are so selective they will inhibit PDGF-R, necessary for the growth of brain cancer cells, but will have no effect on other tumor lines, indicating an ability to be carefully fine-tuned into specific tumor killers.

## Fungi Fighting Back

Just as many bacteria and viruses have become resistant to pharmaceuticals, fungi have been developing drug resistance over the past five years. At the same time, new fungal pathogens are emerging and previously identified rare fungal pathogens are re-emerging, resulting in rising morbidity, mortality, and costs, according to a report by Dennis Dixon,